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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/990,444	11/14/2001	Avi J. Ashkenazi	P2730P1C19	2376

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EXAMINER	
JIANG, DONG	

ART UNIT	PAPER NUMBER
1646	

DATE MAILED: 04/06/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/990,444	ASHKENAZI ET AL.	
	Examiner	Art Unit	
	Dong Jiang	1646	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *14 November 2001*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *119-131* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *119-131* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date *5/24/02*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED OFFICE ACTION

Applicant's preliminary amendment filed on 14 November 2001 is acknowledged and entered. Following the amendment, the original claims 1-118 are canceled, and the new claims 119-131 are added.

Currently, claims 119-131 are pending and under consideration.

Formal Matters:

The title of the invention is not descriptive. A new title is required that is clearly indicative of the invention to which the elected claims are directed.

Objections and Rejections under 35 U.S.C. §112:

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 119-131 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claims 119-124, 127 and 128 recite "the extracellular domain". However, the protein identified as PRO1184 is a secreted protein, and is not disclosed as being expressed on a cell surface. Accordingly, the limitation that the claimed protein comprises the "extracellular domain" is indefinite, as the art does not recognize secreted proteins as having such domains. Further, if the protein had an extracellular domain, the recitation of "the extracellular domain ..., lacking its associated signal sequence" (claim 119, part (d), for example) is indefinite as a signal sequence is not generally considered to be part of an extracellular domain, as signal sequences are cleaved from said domains in the process of secretion from the cell.

The remaining claims are rejected for depending from an indefinite claim.

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 119-124, 127, 128, 130 and 131 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for claims limited in scope to a polypeptide of SEQ ID NO:270, and a polypeptide of SEQ ID NO:270 lacking its associated signal peptide, does not reasonably provide enablement for claims to various % variants SEQ ID NO:270 (claims 119-123, for example), and a fragment of the extracellular domain of SEQ ID NO:2 (claims 119-124, 127 and 128, for example), which do not have a functional activity, or do not have the same functional activity as SEQ ID NO:270. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the invention commensurate in scope with these claims.

The factors considered when determining if the disclosure satisfies the enablement requirement and whether any necessary experimentation is "undue" include, but are not limited to: 1) nature of the invention, 2) state of the prior art, 3) relative skill of those in the art, 4) level of predictability in the art, 5) existence of working examples, 6) breadth of claims, 7) amount of direction or guidance by the inventor, and 8) quantity of experimentation needed to make or use the invention. *In re Wands*, 858 F.2d 731, 737, 8 USPQ2d 1400, 1404 (Fed. Cir. 1988).

The claims are directed to % variants, or a fragment of the extracellular domain thereof, which read on any or all variants meeting the sequence limitation, and encoding polypeptides either with or without a functional activity. The claims encompass an unreasonable number of nucleic acids encoding inoperative polypeptides. However, while the specification teaches that PRO1184 polypeptide of SEQ ID NO:270 is capable of inducing re-differentiation of chondrocytes (Example 159), it provides no guidance or working examples as to how the skilled artisan could use an inactive polypeptide variant or fragment of SEQ ID NO:270, as no functional limitation associated with the variants in the claims. Further, according to the specification, the present PRO1184 is polypeptide a secreted protein, and it is not disclosed as being expressed on a cell surface. As the art does not recognize secreted proteins as having such a domain, one of skilled in the art would not know how to make the claimed invention based upon the instant disclosure, which does not define "the extracellular domain" of the PRO1184 having SEQ ID NO:270.

With respect to the fragment of "the extracellular domain", the specification indicates PRO1184 is a secreted protein, and does not define such a domain, and the art does not recognize secreted proteins as having such a domain. Therefore, it is unclear whether such domain exists, and what kind of functional property it may possess. One of skilled in the art would not know how to make and use the claimed invention based upon the instant disclosure, as the specification provides no definition, guidance or working example regarding such.

Due to the large quantity of experimentation necessary to determine how to make and/or use the inoperative polypeptides, and the fragments of "the extracellular domain", the lack of direction/guidance presented in the specification regarding same, the absence of working examples directed to same, the complex nature of the invention, and the breadth of the claims which embrace a broad class of structurally diverse variants and fragments, undue experimentation would be required of the skilled artisan to make and/or use the claimed invention in its full scope.

Claims 119-124, 127, 128, 130 and 131 are further rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

Claims 119-124, 127, 128, 130 and 131 encompass variant polypeptides having at least 80%, 85%, 90%, 95% or 99% sequence identity with a particular disclosed sequence, such as SEQ ID NO:270 , or "an extracellular domain" of SEQ ID NO:270 (claims 119-124, parts (c) and (d), for example). The claims do not require that the polypeptide possess any particular biological activity, nor any particular conserved structure, or other disclosed distinguishing feature. Thus, the claims are drawn to a genus of polypeptides that is defined only by sequence identity. The specification merely discloses *one* amino acid sequence of human PRO1184 with SEQ ID NO:2. No variants, "an extracellular domain" or other PRO1184 fragments thereof meeting the limitation of the claim were ever identified or particularly described.

To provide adequate written description and evidence of possession of a claimed genus, the specification must provide sufficient distinguishing identifying characteristics of the genus. The factors to be considered include disclosure of compete or partial structure, physical and/or

chemical properties, functional characteristics, structure/function correlation, methods of making the claimed product, or any combination thereof. In this case, the only factor present in the claim is a partial structure in the form of a recitation of percent identity. There is not even identification of any particular portion of the structure that must be conserved. Accordingly, in the absence of sufficient recitation of distinguishing identifying characteristics, the specification does not provide adequate written description of the claimed genus.

Vas-Cath Inc. v. Mahurkar, 19USPQ2d 1111, clearly states that "applicant must convey with reasonable clarity to those skilled in the art that, as of the filing date sought, he or she was in possession *of the invention*. The invention is, for purposes of the 'written description' inquiry, *whatever is now claimed.*" (See page 1117.) The specification does not "clearly allow persons of ordinary skill in the art to recognize that [he or she] invented what is claimed." (See *Vas-Cath* at page 1116).

One cannot describe what one has not conceived. See *Fiddes v. Baird*, 30 USPQ2d 1481 at 1483. In *Fiddes*, claims directed to mammalian FGF's were found to be unpatentable due to lack of written description for that broad class. The specification provided only the bovine sequence.

In the instant application, applicants have a single polypeptide with a specific function that have not been correlated to any particular structural regions. Therefore, only isolated polypeptide comprising the amino acid sequence set forth in SEQ ID NO:270, but not the full breadth of the claims (variants and fragments) meets the written description provision of 35 U.S.C. §112, first paragraph. Applicant is reminded that *Vas-Cath* makes clear that the written description provision of 35 U.S.C. §112 is severable from its enablement provision (see page 1115).

Art:

The prior art made of record and not relied upon is considered pertinent to applicant's disclosure.

Isogai et al. (locus ZDHB-HUMAN, SwissProt_41, 2003) teaches a human polypeptide, which comprises amino acid residues 1-48 of SEQ ID NO:270 of the instant case with 100% homology (see computer printout of the search results).

Conclusion:

No claim is allowed.

Advisory Information:

Any inquiry concerning this communication should be directed to Dong Jiang whose telephone number is 571-272-0872. The examiner can normally be reached on Monday - Friday from 9:30 AM to 7:00 PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Yvonne Eyler, can be reached on 571-272-0871. The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306.

Lorraine Spector

LORRAINE SPECTOR
PRIMARY EXAMINER

Dong Jiang, Ph.D.
Patent Examiner
AU1646
3/30/04